

26.-49. (Previously Cancelled)

50. (New) The method according to claim 21, wherein the PEO has a molecular weight between about 8000 and 15000 Da.

**REMARKS/ARGUMENTS**

**Claim Amendments**

By the present amendment, claim 1 has been amended to delete the limitation that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation of the precursor and instead to specify that the protein- and membrane-compatible sol gel precursor consists essentially of a non-hydrolysed and non-polycondensed organic polyol silane. Support for this amendment is again found, for example, on page 21, lines 28-30 and on page 22, lines 4-22, of the application as filed. In these passages it is clear that, since the preparation of the sol gel requires "adjusting the pH of the aqueous solution of precursor so that formation of a gel occurs" and "[b]y "gel" it is meant a solution or "sol" that has lost flow" and "[t]he sols lose flow due to the hydrolysis and polycondensation of the precursor", the precursor is not hydrolysed or polycondensed prior to the sol gel formation reaction. Further in PCT patent application S.N. PCT/CA03/00790 (publication no. WO 03/2001), which teaches the preparation of organic polyol silanes, the contents of which are incorporated into the present application by reference (see page 14, lines 1-5), it is taught on page 11, lines 4-11, and in the examples, that if "exceptional care was taken to dry the solvents and precursors, it was possible to elicit transesterification to give essentially only Q<sup>0</sup> species – Q refers to various Si(O<sub>4/2</sub>) species. Otherwise transesterification was accompanied by condensation.

Claim 1 has been further amended to specify that the method includes the addition of one or more additives which cause phase separation to occur before gelation of the precursor, wherein the liposome assembly, the one or more additives and the precursor are combined under conditions for the formation of a macroporous silica gel. Support

for this amendment is found, for example, on page 5, lines 7-10, of the application as filed.

Claim 11 has been amended to replace the expression "a liposome assembly" with "the liposome assembly" to improve clarity. This amendment in no way alters the scope of this claim.

Claim 15 has been cancelled.

Claim 16 has been amended to depend on claim 1 in light of the cancellation of claim 15.

Claim 22 has been amended to adjust the lower limit of the molecular weight of PEO to be 8000 kDa as supported by page 15, line 25, of the application as filed.

Claim 50 is new and finds a basis on page 15, line 25, of the application as filed.

The claim amendments have been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants submit that no new matter has been entered by the present amendment and entry of the amendments is respectfully requested.

The Official Action dated March 27, 2007 has been carefully considered. It is believed that the claims and figures submitted herewith and the following comments represent a complete response to the Examiner's comments and place the present application in condition for allowance. Reconsideration is respectfully requested.

#### **Claim Rejections Withdrawn**

The Applicants acknowledge and appreciate the Examiner's withdrawal the rejection of claims 1 and 3-25 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 37, 38, 39, 41, 47, 49, and 51 of

co-pending application no. 10/814,123 in view of Stowell et al. (U.S. Patent No. 6,284,163).

### **Claim Rejections**

#### **35 U.S.C. §103(a)**

The Examiner has rejected claims 1-9, 11 and 14-19 under 35 U.S.C. §103(a) as being unpatentable over by Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001). The Applicants respectively traverse this rejection for the reasons that follow.

In the Examiner's response to the Applicants' arguments filed on January 12, 2007, the Examiner argues that, since the terms "a" and "an" denote "one or more", as taught on page 13, lines 15-16, of the present application as filed, the limitation that the "sol gel precursor is an organic polyol silane" would not exclude the presence of other precursors (i.e. mixed precursors). The Applicants submit that the Examiner's reasoning is in error since, even though the terms "a" and "an" as defined by the present application can mean one or more, this is in reference to the actual feature being claimed. Therefore, the expression "an organic polyol modified silane" would be well understood to mean "one or more organic polyol silanes" not a mixture of different precursors as suggested by the Examiner.

Regardless of the above, the Examiner contends that the method of Gill in view of Gill et al. and Stowell et al. teach the use of a precursor mixture which comprises organic polyol silanes to immobilize liposome assemblies comprising membrane associated molecules. While not agreeing with the Examiner, to expedite the allowance of this case, the Applicants have amended claim 1, and accordingly claims 2-9, 11 and 14-19 dependent thereon, to specify that the precursor "consists essentially of a non-hydrolyzed and non-polycondensed organic polyol silane". Accordingly, the present invention is directed to a method where the precursor of the silica matrix consists essentially of non-hydrolyzed and non-polycondensed organic polyol silane. As argued

in the Applicants' arguments filed on January 12, 2007, at every point in Gill and Gill et al. where it is taught that glycerol may be combined with an alkoxysilane, this combination is only done with an alkoxy silane that is partially or fully hydrolysed into polymeric species. Gil and Gill et al. therefore teach a glycerol-containing sol gel precursor that consists essentially of hydrolyzed and polycondensed silanes.

The Examiner further argues that the limitation of "organic polyol silane that is prepared under conditions to avoid hydrolysis or polycondensation of the precursor" is a product-by-process limitation therefore does not serve to distinguish the precursor utilized in Gil and Gil et al., with that claimed in the present application. While not agreeing with the Examiner, to expedite the allowance of this case, the Applicants have amended claim 1, and accordingly claims 2-9, 11 and 14-19 dependent thereon, to specify that the precursor "consists essentially of a non-hydrolyzed and non-polycondensed organic polyol silane". The Applicants submit that they have now clearly limited the method of the present invention to one that utilizes a precursor that consists essentially of a non-hydrolyzed and non-polycondensed organic polyol silane and that this feature is not taught or suggested in any of the cited art.

Finally, the Examiner comments that the features upon which the Applicants' rely to argue that the cited references fail to show certain features of the Applicants' invention (i.e. the formation of macroporous and mesoporous silica) are not recited in the rejected claims. Again, while not agreeing that this feature is required, to expedite allowance, the Applicants have amended claim 1, and accordingly claims 2-9, 11 and 14-19 dependent thereon, to specify that one or more additives which cause phase separation to occur before gelation of the precursor are combined with the liposome assembly and the precursor under conditions for the formation of a macroporous silica gel. The Applicant submits therefore, that the Examiner's argument that certain distinguishing features of the present invention are not recited in the rejected claims has been rendered moot.

The Applicants submit that they have now amended the rejected claims as suggested by the Examiner and have therefore rendered all of the Examiner's arguments moot. Since all of claims 1-9, 11 and 14-19 require the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules, and since none of the prior art teaches or suggests the existence, let alone the use of such a combination of materials, the Applicant submit that claims 1-9, 11 and 14-19 are in compliance with 35 U.S.C. §103(a).

In light of the above, the Applicants request that the Examiner's rejection of claims 1-9, 11 and 14-19 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claim 10 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claim 9 above, and further in view of Madden (U.S. Patent No. 4,963,287).

Claim 10 depends indirectly on claim 1 and further specifies that the liposome comprises the phospholipid 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC). The Examiner contends that this feature is taught by Madden, therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., a method of forming a liposome assembly using DOPC as taught by Madden in order to form a liposome assembly without harsh treatments and to enhance insertion of membrane proteins and peptides with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claim 10 dependent thereon to require the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the

precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Madden does not teach or suggest the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claim 10 is therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Madden.

In light of the above, the Applicants request that the Examiner's rejection of claim 10 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 12 and 13 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1 and 11 above, and further in view of Lapidot et al. (U.S. PG Pub. No. US 2002/0064541) and Smith et al. (J. Am. Chem. Soc. 2002, 124:4247-4252).

Claims 12 and 13 depend indirectly on claim 1 and further specify that the gel is dried in an aqueous buffer, optionally comprising a humectant (claim 12) or comprising about 5% to about 50 % (v/v) of glycerol (claim 13). The Examiner contends that these features are taught by Lapidot et al. and Smith et al., therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., a use of humectant such as glycerol in a buffer solution as taught by Smith et al. to use during the drying process as taught by Lapidot et al. in order to control the surface nature of the sol gel

matrix and remove ethanol produced during the gelation reaction and during the aging and drying steps with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 12 and 13 dependent thereon to require the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Lapidot et al. and Smith et al. do not teach or suggest the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules, accordingly these references do not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 12 and 13 are therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Lapidot et al. and Smith et al.

The Applicants further note that in the method of the present invention, there is no ethanol produced as a side product, accordingly a person skilled in the art would not have been motivated by the teachings in Smith et al. to utilize glycerol during the washing step.

In light of the above, the Applicants request that the Examiner's rejection of claims 12 and 13 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 20 and 21 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1 and 15-

19 above, and further in view of Keeling-Tucker et al. (Chem. Mater. 2001, 13:3331-3350).

Claims 20 and 21 depend indirectly on claim 1 and further specify that the water soluble polymer is PEO, PEO-NH<sub>2</sub> and polyNIPAM (claim 20) and PEO (claim 21). The Examiner contends that the use of PEO as an additive is taught by Keeling-Tucker et al., therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., the use of the additive PEO as taught by Keeling-Tucker et al. in order to provide segregation into independent phases prior to gelation with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 20 and 21 dependent thereon to require the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Keeling-Tucker et al. do not teach or suggest the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 20 and 21 are therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Keeling-Tucker.

In light of the above, the Applicants request that the Examiner's rejection of claims 20 and 21 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 20-23 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1 and 115-19 above, and further in view of Leung et al. (U.S. Patent No. 6,204,202).

Claims 20-23 depend indirectly on claim 1 and further specify that the water soluble polymer is PEO, PEO-NH<sub>2</sub> and polyNIPAM (claim 20), PEO (claim 21), PEO with a molecular weight of between about 2000-100,000 Da and PEO with a molecular weight of about 10000 Da. The Examiner contends that the use of PEO having a molecular weight in the range of about 200 to 2,000,000 Da as an additive is taught by Leung et al., therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., the use of the additive PEO, in particular with a molecular weight in the range of 2000-100,000 as taught by Leung et al. in order to make silica nanoporous films (such as sol gels) with sufficient mechanical strength that are also optimized to have a desirably low and stable dielectric constant, without the need for further processing to make the film hydrophobic, with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 20-23 dependent thereon to require the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Leung et al. do not teach or suggest the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 20-23 are

therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Leung et al.

The Applicants further note that Leung et al. do not even teach a method involving the combination of a sol-gel precursor with water-soluble polymer to make silica as suggested by the Examiner. Leung et al. instead teach combining a silicon polymer which is a "spin on glass" material with a non-volatile thermally degradable polymer to prepare a mixture which is spin coated onto a substrate and then thermally treated to make silica nanoporous films (See column 3, lines 38-41, and column 4, lines 1-12 of Leung et al.). As the method of Leung et al. is completely unrelated to the methods of Gill, Gill et al., Stowell et al. and the present application, the Applicants submit that a person skilled in the art would not look to the teachings in Leung et al. as relevant to the art of preparing silica using sol-gel techniques.

In light of the above, the Applicants request that the Examiner's rejection of claims 20-23 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 24 and 25 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1, 15 and 16 above, and further in view of Delamarche et al. (Langmuir, 2003, 19:8749-8758).

Claims 24 and 25 depend indirectly on claim 1 and further specify that the additive is a compound of Formula I (claim 24) and a compound of Formula 5 (claim 25). The Examiner contends that the use of PEO-silane in a sol gel polymer ink is taught by Delamarche et al., therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., the use of PEO-silane as taught by Delamarche et al. in order to construct a stable hydrophilic structure with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 24 and 25 dependent thereon to require the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Delamarche et al. do not teach or suggest the use of a precursor that consists essentially of a non-hydrolysed and non-polycondensed polyol silane and an additive that causes phase separation of the precursor before gelation to provide macroporous silica in a method of immobilizing membrane-associated molecules, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 24 and 25 are therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Delamarche et al.

The Applicants further note that Delamarche et al. do not even teach a method involving the combination of a sol-gel precursor with a PEO silane to make silica. Delamarche et al. instead teach grafting a PEO silane on to a polydimethylsiloxane. As the method of Delamarche et al. is completely unrelated to the methods of Gill, Gill et al., Stowell et al. and the present application the Applicants submit that a person skilled in the art would not look to the teachings in Delamarche et al. as relevant to the art of preparing silica using sol-gel techniques.

In light of the above, the Applicants request that the Examiner's rejection of claims 24 and 25 under 35 U.S.C. §103(a) be withdrawn.

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Response dated August 27, 2007  
Reply to Office action of March 27, 2007

Early and favorable action on the merits is awaited. Should the Examiner deem it beneficial to discuss the application in greater detail, the Examiner is invited to contact the undersigned by telephone at (416) 957-1683 at the Examiner's convenience.

Respectfully submitted,

**BERESKIN & PARR**

By   
Patricia Folkins  
Reg. No. 51,933

Bereskin & Parr  
Box 401, 40 King Street West  
Toronto, Ontario  
Canada M5H 3Y2  
Tel: 416-957-1682  
Fax: 416-361-1398